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TITLE

DERIVATIVES OF D-AMINO ACIDS HAVING ANTI-MICROBIAL PROPERTIES

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ABSTRACT OF DISCLOSURE

N-acyl-D-amino acid derivatives having anti-microbial activity, particularly against organisms such as Clostridium botulinum have been developed. These compounds may be used in conjunction and in admixture with other food additives.


FIELD ON THE INVENTION

This invention relates to means of controlling growth of Clostridium botulinum in manufactured or processed foods using N-acyl-D-amino acid derivatives, preferentially in combination with the minimum amounts of sodium nitrite necessary to produce satisfying color and taste.

BACKGROUND TO THE INVENTION

This invention relates to means to control growth of Clostridium botulinum in certain food products. There have been numerous methods designed to control botulinum bacteria [In Mechanism of antimicrobial effect of various food preservatives (Ed. N. Molin), Almquist and Wiksel, Stockholm 1964, p. 10 1]. Sodium nitrite has been widely used for this purpose. [Gray, J.I., and C.J. Randall. J. Food Protection 42, 168 (1979). In the Health Effects of Nitrate, Nitrite and N-Nitroso Compounds. Study by the Committee on Nitrite and Alternative Curing Agents in Foods Part 1. National Academy Press. Washington, D.C. 1981].

The possibility of formation of carcinogenic nitrosamines during cooking of nitrite cured meats led to a search for alternatives to nitrite or an adjunct which would reduce the nitrite content in meats. Some of the promising alternatives include irradiation [Rowley, D.B. et al. J. Food Sci. 20 48, 1016, (1982)] use of Lactobacillus cultures to reduce product pH [Tanaka, N. et al. J. Food Protection 43, 450, (1980)] use of sulfur dioxide [Tompkin, R.B. et al. Appl. Environ. Microbiol. 39, 1096,



(1980)] use of sodium hypophosphite [Banner, R.J. Food Engineering 53 130, (1980)] and fumarate esters (huntanen, C.N. 41st Annual Meeting of Institute of Food Technologists. June 1981. Atlanta Ga.) One of the most efficient agents proposed as a partial sodium nitrite replacement is potassium sorbate or sorbic acid [Sofos, J.N. and Busta, F.F. Food Technol. 24, 244 (1980), Busta, F.F. Food Technol. of Australia 34, 529 (1982)], Blocher, J.C. et al, J. Food Sci. 47, 405 (1981)]. Ueno, R.N. et al. U.S. Pat. 4,299,852 (1981), Ueno, R.N. et al, U.S. Pat. 4,342,789 (1982).

10 However, recent reports show that mutagenicity was detected in some food preparations cured with the sorbic acid-sodium nitrite mixtures [Khoudokormoff, B. International Symposium on the Chemical Toxicology of Food. June 1978. Milan, Italy. Khoudokormoff, B. Fed. Cosmet. Toxicol. 19, 405-407 (1981)]. Reports on mutagenicity of sorbic acid itself in wine and curing brines have also emerged [Lafout, M.G. and Lafout, S.P. Med. Nutr. 15, 195 (1979)]. There is, therefore a need for the preservatives which do not have these side effects.

20 This invention provides N-acylamino acids of the formula:



wherein X, when taken in conjunction with the CO group, is an acyl moiety and Y, when taken in conjunction with the NH group, is a D-amino acid or glycine moiety, or a foodstuff acceptable salt thereof, other than glycyl D-alanine, acetyl D-tryptophan, acetyl D-methionine, acetyl D-valine and acetyl D-alanine.

Preferably X does not contain any NH_2 groups and

preferably the carbon atom of the carbonyl group is attached to another carbon atom. X may be a saturated moiety, so that, for example, XCO may be lauroyl, myristoyl or palmitoyl, or X may be unsaturated so that XCO is, for example, sorbyl.

X is preferably, selected from the group consisting of sorbyl or fatty acyl (C8-C24). Y is preferably an α -D-amino acid and suitable examples can be selected from the group consisting of D-alanine, D-tryptophan, D-methionine, D-valine and D-aspartic acid.

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This invention also provides salts of such compounds suitable for use in foodstuffs. Mention is made of alkali metal and alkaline earth metal salts, of which sodium and potassium salts are generally preferred.

Compounds of the above referenced type may be used in combination with a food product and when so employed preferably present at a concentration of at least 2,600 ppm by weight. Such compounds may be used in combination with food grade nitrites.

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The invention therefore also provides a composition according to claim 26 wherein the active ingredient comprises N-sorbyl-D-tryptophan, N-sorbyl-D-alanine, N-sorbyl-D-valine, N-sorbyl-D-methionine, N-sorbyl-D-aspartic acid, Palmitoyl-D-tryptophan, Myristoyl-D-aspartic acid or Hexanoyl-D-alanine.

These compounds may further be used in methods for control of microorganisms in food products, particularly meat-containing products and especially red meat-containing products. Such a method comprises incorporating at least about 2600 ppm of such a compound to such a food product. In such a compound the

X - CO group is preferably sorbyl and the NH - Y group is preferably D-tryptophan. The compound is preferably, combined with addition of 60 ppm of sodium nitrite to enhance activity and to maintain desirable colour and taste for consumers satisfaction. The above compound has additional advantage of being stable towards intestinal peptidases which suggests that such food additive will not be metabolized.

Preferred means for practising the invention comprise:

10 (a) acylation of D-amino acids by sorbic acid, succinimidyl esters or any other active ester such pentachlorophenyl, pentafluorophenyl, or by sorbyl chloride or sorbic anhydride.

(b) recovering the N-sorbylamino acid as product.

(c) incorporating the derivative or the salt (sodium or potassium thereof) optionally in combination with sodium nitrite, in to a desired processed or manufactured food product such food product being for example sausages, canned minced meat products, corned beef, luncheon meats, meat products comminuted and stuffed into casings.

20 It can be seen that the present invention describes the advantageous use of non-mutagenic amino acid derivatives of sorbic acid as potent food preservatives. Such use represents replacement of the application of high levels of sodium nitrite (150 ppm) or the potentially mutagenic mixture of

potassium sorbate and sodium nitrite. The named compounds are easily and inexpensively obtainable, stable at any pH or temperature in most food applications where preservation against Clostridium botulinum outgrowth is required.

DETAILED DESCRIPTION OF THE INVENTION

CHEMICAL SYNTHESSES

Material and methods

Melting points (uncorrected) were taken by the capillary method. The NMR spectra were recorded on a Varian T-60 spectrometer. Optical rotations were determined on Perkin-Elmer 141 polarimeter. Amino acids were purchased from Sigma Chemical Company (Saint Louis, Missouri, U.S.A.). Characterizing data for some compounds of the invention are given in Table 1.

Succinimidyl sorbate

To a suspension of N-hydroxysuccinimide (36.87g, 0.32 mole) and sorbic acid (35.92g, 0.32 mole) in methylene chloride (200mL) was added 1-ethyl-3-(3-dimethylaminopropyl) carbodiimide (61.42g, 0.32 mole) dissolved in methylene chloride (140mL). The mixture was stirred at room temperature for 3 hours and then kept overnight at 0°C. The mixture was extracted 3 times with 10% citric acid, 3 times with saturated sodium bicarbonate solution and with water till neutrality. The semicrystalline residue (66.0g, 98.6%) was recrystallized from methylene chloride-diethyl ether giving 55.0 and 5.2g (91.4%) of the crystalline title compound. M.p. 104°C. Analysis calculated for $C_{10}H_{11}NO_4$ (209.18): C, 57.4; H, 5.3; N, 6.7. Found: C, 57.0; H,

5.5, N. 6.5%.

NMR, : 7.46 (1H, m, C3), 6.33 (2H, m, C4 and C5), 5.93 (1H, d, C2), 2.88 (4H, s, 2CH₂ succinimidyl moiety), 1.9 (3H, d, CH₃) (CDCl₃).

Sorbyl-D-tryptophan

To a suspension of D-tryptophan (20.43g, 0.1 mole) and sodium bicarbonate (12.6g, 0.15 mole) in water (200mL) and acetone (100mL) was added succinimidyl sorbate (20.92g, 0.1 mole) in acetone (100mL) in 3 portions. The reaction mixture was stirred at room temperature overnight, acidified to pH 4.5 and acetone removed by distillation. The pH was adjusted to 2, the crystalline product was separated by filtration, washed with distilled water (till neutrality of the filtrate) and recrystallized from the mixture of ethanol with water giving 25.92g (87%) of the title compound.

DEMONSTRATION OF UTILITY OF THE COMPOUNDS

Materials and Methods

Organism

Five type A strains of Clostridium botulinum, 6A, 17A, 62A, CK2A, and 317121A, and five type B strains, 1B1, 368B, 462B, 13982B and MRB were used throughout these studies. Spores were prepared by the method of Schmidt et al. [J. Food Sci. 27, 77 (1962)] and enumerated on Wynne agar supplemented with egg yolk [Hauschild, A.H.W. et al. J. Food Prot. 45, 500 (1982)].

Meat Slurries

To fresh minced pork meat two parts of 3% NaCl solution were added to

obtain a final concentration of 2% brine. Compounds to be tested were added in powdered form as potassium salts to the slurries in final amounts of 0.26%. A mixture of approximately 200 botulinum spores were added per 1mL of slurry unless indicated otherwise. The spore mixture comprised an approximately equal number of each of the five type A and five type B strains of C. botulinum. The meat slurry was blended for one minute, the pH adjusted (values indicated at the tables), and blended for an additional minute. Then the slurry was dispensed in 10 ml volumes to sterile 16 X 150mm test tubes, processed to 70°C, cooled and sealed as described by Rayman et al [App. Environ. Microbiol. 41, 375 (1981)]. Five tubes of slurries were abused by incubating at 25°C for 56 days or until growth was observed as evidenced by gas production.

Antibotulinal effect of N-acyl-D-amino acids

A series of N-acyl-D-amino acids were tested using the above described technique in the presence or absence of 60 ppm of sodium nitrite: it can be seen that derivatives of D-tryptophan in conjunction with 60 ppm of sodium nitrite, as well as myristoyl-D-aspartic acid and glycyl-D-alanine exhibited the highest inhibition. The results are presented in Table 2.

Comparison of the activity of sorbyl-D-tryptophan with its L-isomer

Meat slurries were treated with 0.26% of either sorbyl-D-tryptophan or sorbyl-L-tryptophan converted into potassium salts. The results in Table 3 indicate superior inhibition of spore outgrowth by the N-acyl-D-amino acid derivative; sorbyl-D-tryptophan inhibited outgrowth over the entire 56 days of abuse, whereas, its L-isomer inhibited outgrowth for an average of 11 days which was only slightly longer than 60 ppm nitrite alone or in combination with 0.26% D-tryptophan.

Comparison of the activity of sorbyl-D-tryptophan with control experiments.

Results of the control experiments carried out with 150 ppm of sodium nitrite and 0.26% of potassium sorbate are shown in the Table 4.

Effect of pH on inhibition of spore outgrowth

Sorbyl-D-tryptophan which showed the greatest inhibition of spore outgrowth, was selected for further testing. This compound at a final concentration of 0.26% was added individually to inoculated pork slurries containing 60 ppm nitrite and adjusted to pH 5.8 or 6.0. The results in Table 5 indicate a decrease in effectiveness of the compound to inhibit spore outgrowth as the pH increased.

Contribution of D-tryptophan to inhibitory activity

The sorbic acid and D-tryptophan moieties contribute 32.46% and 59.12% of the weight respectively to sorbyl-D-tryptophan. The experiments shown in Table 6 were performed to determine whether the moieties separately and in proportions equivalent to those present in the N-acylamino acid compound would effect the same degree of spore outgrowth inhibition as the derivatized amino acids. The results indicate a reduction in the inhibitory effects of the individual moieties applied as potassium salts in such final concentration in the slurries which corresponded to their molar proportions in the N-acylamino acid molecule and supplying altogether 0.26% of the growth inhibitor.

EXAMINATION OF MUTAGENIC
POTENTIAL OF THE COMPOUNDS
UNDER STUDY

Compounds of this type with this utility should be examined for mutagenic potential as part of the process of selection of a preferred compound or set of compounds.

Materials and methods

10 The salmonella/microsome assay was used for this study according to Mason, D.M. and Ames, B.N. Mut. Research 113, 173, 1983. A modification of the standard plate incorporation assay, the so-called "preincubation" assay was also employed. In this method the bacteria and test chemicals were preincubated for 20 minutes at 37°C before plating. Salmonella typhimurium strains TA 97, TA 98 and TA 100 were used. For metabolic activation, liver homogenates prepared from rats induced with aroclor 1254 were employed. Results are expressed as average number of revertant colonies per plate calculated from duplicate assay plates.

20 The results of the mutagenicity assays on the test compounds are presented in Tables 7a, 7b. All test substances gave negative responses, i.e., no increases in the number of revertants above the negative control (solvent) were observed. Table 7c shows the positive mutagens employed with each assay and their mutagenic activities.

Table 1

N-SORBYL-D-AMINO ACID DERIVATIVES

Amino acid	m.p. (°C)	$[\alpha]_D^{23}$ ^a	Formula	calcd C H	Anal N	found C H N
tryptophan ^b	110-112	-80.3°	C ₁₇ H ₁₈ N ₂ O ₃	66.43 6.55	9.11	66.24 6.31 9.38
alanine	140	+36.3°	C ₉ H ₁₃ N O ₃	59.00 7.15	7.64	59.45 7.07 7.73
valine	168-169°	+2.2°	C ₁₁ H ₁₇ n O ₃	62.54 8.11	6.63	62.94 8.52
methionine	112-113.5	+4.2°	C ₁₁ H ₁₇ N O ₃	54.29 7.04	5.75	54.67 7.29 5.80
aspartic acid	117-179°	-8°	C ₁₀ H ₁₃ N O ₅	52.86 5.76	6.16	52.99 5.50 6.19

The preparation of the compounds was carried out essentially as described for the synthesis of sorbyl-D-tryptophan.

^a determined in ethanol

^b C, H, N content calculated with 1/2 mol of water.

Table 1 (cont'd)

VARIOUS N-ACYL-AMINO ACID DERIVATIVES

Amino acid	m.p. (°C)	$[\alpha]_D^{23}$ ^a	Formula	calcd $\frac{C}{H}$	Anal $\frac{N}{H}$	found $\frac{C}{H}$	N
Pal-D-Try	98-100	-15.7	C ₂₇ H ₄₂ N ₂ O ₃	73.26	9.56	72.82	9.31
Myr-D-Asp	116-118	-5.4	C ₁₈ H ₃₃ N O ₅	62.13	9.46	62.10	9.46
Hex-D-Ala	141	+39.7°	C ₉ H ₁₇ N O ₃	57.73	9.15	57.50	9.30

The preparation of the compounds was carried out essentially as shown for the synthesis of sorbyl-D-tryptophan
^a determined in ethanol

^b C, H, N content calculated with 1/4 mol of water.

Table 2

INHIBITION OF C. BOTULINUM SPORE OUTGROWTH BY SOME N-ACYL-D-AMINO ACIDS

Compound (0.26%)	Nitrite present (60 ppm)		Nitrite absent No. of days for growth which occurred in all tubes
	Range of days for growth	Average no. of days for growth	
Sorbyl-D-tryptophan (6)*	11 - >56	27	8
Acetyl-D-tryptophan (2)	16 - >56	29	6
Palmitoyl-D-tryptophan (1)	28 - 34	33	7
Sorbyl-D-methionine (1)	9 - 15	13	12
Acetyl-D-methionine (1)	9 - 20	14	6
Sorbyl-D-valine (1)	9 - 20	17	not done
Acetyl-D-valine (1)	all 5 tubes in 6 days		6
Sorbyl-D-aspartic acid (1)	all 5 tubes in 6 days		6
Myristoyl-D-aspartic acid (1)	9 - >56	36	7
Hexanoyl-D-alanine (1)	9 - 16	10	7
Acetyl-D-alanine (1)	all 5 tubes in 7 days		7
Glycyl-D-alanine (2)	5 - >56	27	7
Potassium sorbate (10)	9 - >56	18	7

* Numbers in parenthesis represent the amount of experiments carried out with each compound (each experiment comprised five tubes of meat slurry).

Table 3

Antibotulinal effect of N-acyl-D-amino acid and
N-acyl-L-amino acid derivatives*

Amino acid derivative ***	Nitrite (60ppm)	Average no. of days for growth **
None	-	5
None	+	7
Sorbyl-L-tryptophan	+	11
Sorbyl-D-tryptophan	+	>56
D-tryptophan	+	8

* Pork slurries inoculated with approximately 100 mixed botulinum spores per ml contained 2% NaCl and processed to 70°C pH 5.8.

** Five tubes of slurry were used for each treatment.

*** In the form of potassium salt and in the final concentration of 0.26%.

Table 4

Comparison of the activity of sorbyl-D-tryptophan,
potassium sorbate and 150 ppm of sodium nitrite
on inhibition of spore outgrowth.

Compound tested*	Range of days for growth	Av. no. of days for growth **
Sorbyl-D-tryptophan	11->56	27 (6) ***
Potassium sorbate	9->56	18 (10)
150 ppm of sodium nitrite	22->56	39 (1)

* Pork slurries inoculated with approximately 200 mixed botulinum spores per 1 ml. contain 2% NaCl and, except for the 150 ppm nitrite treatment, 60 ppm of sodium nitrite and 0.26% of the compound under test.

** To calculate number of days, >56 was taken as 56 days for growth to occur.

*** Numbers in parentheses represent the number of experiments from which the average number of days was calculated.

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Table 5

Comparison of the activity of sorbyl-D-tryptophan, potassium sorbate and 150 ppm of sodium nitrite at different pH values on inhibition of spore outgrowth.

Compound tested *	pH of pork slurry	Range of days for growth	Av. no. of days for growth **
Sorbyl-D-tryptophan	5.8	11->56	27 (6)***
	6.0	6-41	18 (4)
Potassium sorbate	5.8	9->56	18 (10)
	6.0	7-12	10 (2)
150 ppm nitrite	5.8	22->56	39 (1)
	6.0	20->56	30 (1)

* Pork slurries inoculated with approximately 200 mixed botulinum spores per 1 mL contained 2% NaCl and, except for the 150 ppm nitrite treatment, 60 ppm nitrite and 0.26% of a compound.

** To calculate average number of days, >56 was taken as 56 days for growth to occur.

*** Numbers in parentheses represent the number of experiments from which the average number of days was calculated.

Table 6

Effect of N-acylamino acid derivatives and individual constituents thereof on inhibition of spore outgrowth *

<u>Compound tested ***</u>	<u>Range of days for growth</u>	<u>Av. no. of days for growth **</u>
Sorbyl-D-tryptophan	11->56	24
Potassium sorbate	8-13	10
Potassium sorbate (0.10%) plus D-tryptophan (0.16%)	8-11	10

* Pork slurries inoculated with approximately 200 mixed botulinum spores per ml contain 2% NaCl and 60 ppm nitrite, pH 5.8.

** See footnote to Table 3.

*** The first two compounds were used at a final concentration of 0.26%.

Table 7a

Mutagenic Assay of Sorbyl D-tryptophan

Concentration µg/plate	Revertants/plate					
	TA 97		TA 98		TA 100	
	-	+S9	-	+S9	-	+S9
Sample 1						
	standard assay					
0 water	138	242	28	27	118	127
100	127	179	27	27	132	113
500	122	252	24	30	136	115
1000	122	269	32	25	117	112
2000	119	206	23	27	111	109
Sample 2						
	standard assay					
0 water	137	154	24	41	167	136
500	131	142	33	38	166	132
1000	119	131	23	39	160	145
2000	138	154	24	36	157	133
2500	110	139	35	36	157	126
	preincubation assay					
0 water	116	123	31	38	153	144
500	114	118	24	39	158	146
1000	108	125	25	39	150	148
2000	116	139	24	48	150	160
2500	99	117	29	41	157	157

Preincubation - 20 min at 37°C

Table 7b

Mutagenic Assay of Potassium Sorbate and Glycyl-D-alanine

Concentration μg/plate	Revertants/plate					
	TA 97		TA 98		TA 100	
	+S9		+S9		+S9	
K ⁺ sorbate						
0 water	138	286	28	27	118	127
100	136	284	29	27	114	109
500	128	319	24	30	112	120
1.000	166	292	19	19	116	105
5.000	218	274	15	24	99	92
gly-D-ala						
100	145	248	31	31	110	130
500	141	180	30	25	105	120
1.000	135	322	23	22	147	130
5.000	113	176	18	24	123	139

X

Table 7c

Mutagenic Assay of Positive Control Substances

Chemical	Concentration $\mu\text{g}/\text{plate}$	Bacterial strain	Metabolic activation	Revertant/ plate
sodium azide	10	TA 100	—	1706
4-nitro-1,2- phenylenediamine	10	TA 97	—	835
2-nitrofluorene	100	TA 98	—	2055
Benzo(a)pyrene	5	TA 97	+	589
		TA 98	+	417
		TA 100	+	361

For metabolic activation aroclor induced rat liver homogenate was used.

From these results, it is concluded that potassium sorbate, glycyl-D-alanine, sorbyl-D-tryptophan, are not mutagenic in the Salmonella/microsome assay.

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THE EMBODIMENTS OF THE INVENTION IN WHICH AN EXCLUSIVE PROPERTY OR PRIVILEGE IS CLAIMED ARE DEFINED AS FOLLOWS:

1. An N-acylamino acid of the formula:

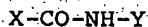


wherein X when taken in conjunction with the CO group, is an acyl moiety and Y when taken in conjunction with NH group, is a D-amino acid or glycine moiety, or a foodstuff acceptable salt thereof, other than glyceryl D-alanine, acetyl D-tryptophan, acetyl D-methionine, acetyl D-valine and acetyl D-alanine.

2. The compound of claim 1 wherein the acyl moiety has from 8 to 24 carbon atoms.

3. The compound of claim 1 wherein XCO is selected from the group consisting of sorbyl-, lauroyl-, and myristoyl-, and palmitoyl-groups and Y, together with the NH group, is selected from the group consisting of D-alanine, D-tryptophan, glycine, D-valine and D-aspartic acid.

4. A composition comprising an N-acylamino acid of the formula:

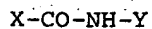


wherein X when taken in conjunction with the CO group, is an acyl moiety and Y when taken in conjunction with the NH group is a D-amino acid or glycine moiety, or a suitable salt thereof, in combination with a selected food product.

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5. The composition of claim 4 wherein at least 2600 ppm of the N-acylamino acid is present.

6. A composition comprising an N-acylamino acid of the formula:



wherein X, when taken in conjunction with the CO group, is an acyl moiety and Y, when taken in conjunction with the NH group is a D-amino acid or glycine moiety, or a suitable salt thereof, in combination with a food grade nitrite.

7. A food product in combination with the composition of claim 6 wherein at least about 2600 ppm of the N-acyl-D-amino acid is present.

8. The food product of claim 7 wherein at least about 60 ppm of food grade nitrite is present.

9. The compound of claim 1 in salt form with sodium or potassium.

10. N-sorbyl-D-tryptophan.

11. N-sorbyl-D-alanine.

12. N-sorbyl-D-valine.

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13. N-sorbyl-D-methionine.
14. N-sorbyl-D-aspartic acid.
15. Palmitoyl-D-tryptophan.
16. Myristoyl-D-aspartic acid.
17. Hexanoyl-D-alanine.
18. A method for control of microorganisms in a food product comprising incorporating an effective amount of an N-acyl-amino acid of the formula:
- $$X-CO-NH-Y$$
- wherein X, when taken in conjunction with the CO group, is an acyl moiety and Y, when taken in conjunction with the NH group is a D-amino acid or glycine moiety, or a suitable salt thereof, to said food product.
19. The method of claim 18 wherein said food product is a meat-containing product.
20. The method of claim 19 wherein said meat containing product is a canned minced meat product.
21. The method of claim 19 wherein the said meat product is a comminuted meat product stuffed in casings.

LB

22. The method of claim 19 wherein the said meat product is sausage.

23. The method of claim 19 wherein said meat-containing product is a red-meat containing product, the compound is selected from the group having an acyl moiety selected from sorbic acid or a fatty acid having a C₈-C₂₄ chain and a D-amino acid moiety selected from D-alanine, D-tryptophan, D-methionine, D-valine and D-aspartic acid.

24. The method of claim 22 wherein said N-acylamino acid is incorporated in combination with a food grade nitrite.

25. A process for preparing an N-acyl-D-amino acid according to claim 1 which comprises acylating of a selected D-amino acid.

26. A food- or feed-acceptable composition comprising an N-acylamino acid of the formula:



wherein X when taken in conjunction with the CO group, is an acyl moiety, and Y when taken in conjunction with the NH group is a D-amino acid or glycine moiety, or a food- or feed-acceptable salt thereof, as an active ingredient, in combination with a further active ingredient or a food- or feed-acceptable diluent or carrier.

27. A composition according to claim 26 wherein XCO is

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selected from the group consisting of sorbyl-, lauroyl-, and myrisotyl-, and palmitoyl-groups and Y, together with the NH group, is selected from the group consisting of D-alanine, D-tryptophan, glycine, D-valine and D-aspartic acid.

28. A composition according to claim 26 wherein in the active ingredient the acyl moiety is selected from sorbic acid or a fatty acid having a C₈-C₂₄ chain and a D-amino acid moiety selected from D-alanine, D-tryptophan, D-methionine, D-valine and D-aspartic acid.

29. A composition according to claim 26 wherein the active ingredient comprises N-sorbyl-D-tryptophan, N-sorbyl-D-alanine, N-sorbyl-D-valine, N-sorbyl-D-methionine, N-sorbyl-D-aspartic acid, Palmitoyl-D-tryptophan, Myristoyl-D-aspartic acid or Hexanoyl-D-alanine.

SMART & BIGGAR
OTTAWA, CANADA
PATENT AGENTS

B

